# IN THE UNITED STATES PATENTAND TRADEMARK OFFICE

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| In Re: | U.S. Patent No. 6,034,239 |
| Issued: | Mar. 7, 2000 |
| To: | Shigenori OHKAWA et. al. |
| For: | Tricyclic Compounds, Their Production and Use |
| From: | Serial No. 08/812,168 |
| Filed: | Mar. 6, 1997 |

**MAIL STOP: PATENT EXTENSION**

Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450

Sir:

## CERTIFICATION

It is hereby certified that this is a true and complete duplicate copy of the Application for Extension of the Term of United States Patent No. 6,034,239 submitted concurrently herewith including Exhibits A - K.

Respectfully submitted,

Dated: September 6, 2005

(847)383-3372
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**MAIL STOP: PATENT EXTENSION**
Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450
Sir:

## TRANSMITTAL LETTER

1. Enclosed is an Application for Extension of the Term of United States Patent No. 6,034,239 submitted concurrently herewith including Exhibits A - K

2. Two (2) True and Correct duplicate copies of said Application and Exhibits A-K.

3. The Commissioner is authorized to charge the prescribed fee of $1,120.00 (37 CFR 1.17(j)(1) – USPTO Fee CODE 1457), and any other required fees, or to credit any overpayments to Applicant's USPTO Deposit Account No. 500 799 (Takeda Pharmaceutical Company Inc.).

Respectfully submitted,

Dated: September 6, 2005

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# IN THE UNITED STATES PATENTAND TRADEMARK OFFICE

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**MAIL STOP: PATENT EXTENSION**

Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450

Sir:

**APPLICATION FOR EXTENSION OF PATENT TERM OF UNITED STATES PATENT NO. 6,034,239 UNDER 35 U.S.C. §156**

Your applicant, TAKEDA PHARMACEUTICAL COMPANY LTD. ("TAKEDA"), formerly doing business by the name TAKEDA CHEMICAL INDUSTRIES, LTD., a corporation organized under the laws of Japan, having its principal place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka, Japan, represents that it is the owner of the entire right, title and interest in and to Letters Patent of the United States No. 6,034,239 granted to Shigenori OHKAWA, Osamu UCHIKAWA, Kohji FUKATSU, and Masaomi MIYAMOTO on the 7th day of March, 2000, for TRICYCLIC COMPOUNDS, THEIR PRODUCTION AND USE by virtue of an assignment recorded in the United States Patent and Trademark Office on March 6, 1997 at Reel 008433, Frame 0452.

A copy of the assignment and the USPTO Notice of Recordation is attached hereto as EXHIBIT A. Documentation of the change of name of the assignee was recorded in the United States Patent and Trademark Office on January 19, 2005 at Reel 015612, Frame 0101. A copy of the USPTO Notice of Recordation of name change is attached hereto as EXHIBIT B.

U.S. Patent No. 6,034,239, for which an extension of the patent term is sought, is presently in force and is not subject to any disclaimer. Accordingly, U.S. Patent No. 6,034,239 is scheduled to expire on March 6, 2017, i.e. 20 years from the earliest claimed U.S. priority date for the application for patent under 35 U.S.C. §154.

Pursuant to the provisions of 37 C.F.R. §1.730, your applicant hereby applies for an extension of the term of said United States patent of 808 days under 35. U.S.C. §156.

The patent term extension which is hereby requested is supported by the materials set forth herewith in the accompanying papers. In the materials which follow herein, paragraph numbers correspond to the paragraph numbers in 37 C.F.R. §1.740(a).

(1) The approved product is ROZEREM™ (ramelteon) Tablets 8 mg for the treatment of insomnia characterized by difficulty with sleep onset. A complete identification of the approved product is attached hereto as EXHIBIT C.

(2) ROZEREM™ was subject to regulatory review under section 505(b) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §355).

(3) ROZEREM™ received permission for commercial marketing or use under section 505 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §355) on July 22, 2005. A copy of the FDA approval letter is attached as EXHIBIT D.

(4) The active ingredient in ROZEREM™ is ramelteon. Said active ingredient has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act or the Virus-Serum-Toxin Act.

(5) This application is being submitted within the sixty-day period permitted for its submission pursuant to 37 C.F.R. §1.720(f). The last day on which this application could be submitted is September 20, 2005.

(6) The U.S. patent for which an extension is being sought is identified as follows:

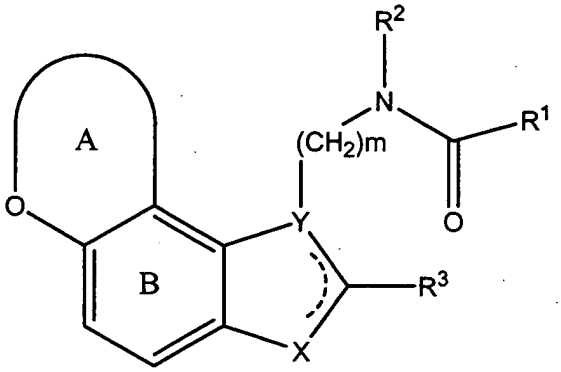
| | |
|---|---|
| Inventors: | Shigenori Ohkawa, Osamu Uchikawa, Kohji Fukatsu and Masaomi Miyamoto |
| Patent No: | 6,034,239 |
| Title: | Tricyclic Compounds, Their Production and Use |
| Issued: | March 7, 2000 |
| Expires: | March 6, 2017 |

(7) A complete copy of United States Patent No. 6,034,239, the patent for which an extension is being sought, is attached hereto as EXHIBIT E.

(8) No terminal disclaimer has been filed. No certificate of correction or reexamination certificate has issued for United States Patent No. 6,034,239. A copy of the USPTO maintenance fee statement is attached hereto as EXHIBIT F.

(9) United States Patent No. 6,034,239 claims the approved product ROZEREM™, methods of using ROZEREM™, and methods for making it as follows:

CLAIM 1 of United States Patent No. 6,034,239 claims a compound of the formula:




wherein $R^1$ represents an optionally substituted hydrocarbon group, an optionally substituted amino group or an optionally substituted heterocyclic group;

$R^2$ represents a hydrogen atom or an optionally substituted hydrocarbon group;

$R^3$ represents a hydrogen atom, an optionally substituted hydrocarbon group, or an optionally substituted heterocyclic group;

X represents $CHR^4$, $NR^4$, O or S in which $R^4$ represents a hydrogen atom or an optionally substituted hydrocarbon group;

Y represents C, CH or N, provided that when X is $CH_2$, Y is C or CH;

------ represents a single bond or a double bond;

ring A represents an optionally substituted, 5- to 7-membered oxygen-containing heterocyclic ring;

ring B represents an optionally substituted benzene ring; and

m represents an integer of 1 to 4, or a salt thereof.

The compound of the above formula is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 1 covers the approved product.

CLAIM 2 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein:

$R^1$ is (i) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkylcarbamoyl, di-$C_{1-6}$ alkylcarbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino,

(ii) an amino group which may be substituted by 1 or 2 substituents selected from the group consisting of a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl and $C_{6-14}$ aryl group, each of which may be substituted by 1 to 5 substituents selected

from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di-$C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino, or

(iii) a 5- to 14-membered heterocyclic group containing, besides carbon atoms, 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, which group may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{2-6}$ alkynyl, $C_{2-6}$ alkenyl, $C_{7-11}$ aralkyl, $C_{6-10}$ aryl, $C_{1-6}$ alkoxy, $C_{6-10}$ aryloxy, formyl, $C_{1-6}$ alkyl-carbonyl, $C_{6-10}$ aryl-carbonyl, formyloxy, $C_{1-6}$ alkyl-carbonyloxy, $C_{6-10}$ aryl-carbonyloxy, carboxyl, $C_{1-6}$ alkoxy-carbonyl, $C_{7-11}$ aralkyloxy-carbonyl, carbamoyl, an optionally halogenated $C_{1-4}$ alkyl, oxo, amidino, imino, amino, mono- $C_{1-4}$ alkylamino, di-$C_{1-4}$ alkylamino, 3- to 6-membered cyclic amino, $C_{1-3}$ alkylenedioxy, hydroxy, nitro, cyano, mercapto, sulfo, sulfino, phosphono, sulfamoyl, mono-$C_{1-6}$ alkylsulfamoyl, di-$C_{1-6}$ alkylsulfamoyl, $C_{1-6}$ alkylthio, $C_{6-10}$ arylthio, $C_{1-6}$ alkylsulfinyl, $C_{6-10}$ arylsulfinyl, $C_{1-6}$ alkylsulfonyl and $C_{6-10}$ arylsulfonyl;

$R^2$ is (i) a hydrogen atom or (ii) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di- $C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl- carbonylamino;

$R^3$ is (i) a hydrogen atom, (ii) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di- $C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl- carbonylamino or

(iii) a 5- to 14-membered heterocyclic group containing, besides carbon atoms, 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, which group may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{2-6}$ alkynyl, $C_{2-6}$ alkenyl, $C_{7-11}$ aralkyl, $C_{6-10}$ aryl, $C_{1-6}$ alkoxy, $C_{6-10}$ aryloxy, formyl, $C_{1-6}$ alkyl-carbonyl, $C_{6-10}$ aryl-carbonyl, formyloxy, $C_{1-6}$ alkyl-carbonyloxy, $C_{6-10}$ aryl-carbonyloxy, carboxyl, $C_{1-6}$ alkoxy-carbonyl, $C_{7-11}$ aralkyloxy-carbonyl, carbamoyl, an optionally halogenated $C_{1-4}$ alkyl, oxo, amidino, imino, amino, mono- $C_{1-4}$ alkylamino, di-$C_{1-4}$ alkylamino, 3- to 6-membered cyclic amino, $C_{1-3}$ alkylenedioxy, hydroxy, nitro, cyano, mercapto, sulfo, sulfino, phosphono, sulfamoyl, mono-$C_{1-6}$ alkylsulfamoyl, di-$C_{1-6}$ alkylsulfamoyl, $C_{1-6}$ alkylthio, $C_{6-10}$ arylthio, $C_{1-6}$ alkylsulfinyl, $C_{6-10}$ arylsulfinyl, $C_{1-6}$ alkylsulfonyl and $C_{6-10}$ arylsulfonyl;

$R^4$ is (i) a hydrogen atom or (ii) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-16}$ alkyl-

carbamoyl, di-$C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl- carbonylamino;

ring A is a 5- to 7-membered heterocyclic group optionally containing, besides carbon atoms and an oxygen atom, 1 to 3 hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, which group may be substituted by 1 to 4 substituents selected from the group consisting of (i) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy- carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di-$C_{1-6}$ alkyl- carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino, (ii) a halogen, (iii) $C_{1-6}$ alkoxy, (iv) $C_{6-10}$ aryloxy, (v) formyl, (vi) $C_{1-6}$ alkyl-carbonyl, (vii) $C_{6-10}$ aryl-carbonyl, (viii) formyloxy, (ix) $C_{1-6}$ alkyl-carbonyloxy, (x) $C_{6-10}$ aryl- carbonyloxy, (xi) carboxyl, (xii) $C_{1-6}$ alkoxy-carbonyl, (xiii) $C_{7-11}$ aralkyloxy-carbonyl, (xiv) carbamoyl, (xv) an optionally halogenated $C_{1-4}$ alkyl, (xvi) oxo, (xvii) amidino, (xviii) imino, (xix) amino, (xx) mono-$C_{1-4}$ alkylamino, (xxi) di-$C_{1-4}$ alkylamino, (xxii) 3- to 6-membered cyclic amino, (xxiii) $C_{1-3}$ alkylenedioxy, (xxiv) hydroxy, (xxv) nitro, (xxvi) cyano, (xxvii) mercapto, (xxviii) sulfo, (xxix) sulfino, (xxx) phosphono, (xxxi) sulfamoyl, (xxxii) mono-$C_{1-6}$ alkylsulfamoyl, (xxxiii) di-$C_{1-6}$ alkylsulfamoyl, (xxxiv) $C_{1-6}$ alkylthio, (xxxv) $C_{6-10}$ arylthio, (xxxvi) $C_{1-6}$ alkylsulfinyl, (xxxvii) $C_{6-10}$ arylsulfinyl, (xxxviii) $C_{1-6}$ alkylsulfonyl and (xxxix) $C_{6-10}$ arylsulfonyl; and

ring B is a benzene ring which may be substituted by 1 or 2 substituents selected from the group consisting of

(i) a halogen,

(ii) a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl or $C_{6-14}$ aryl group which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di-$C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino,

(iii) an amino group which may be substituted by 1 or 2 substituents selected from the group consisting of a $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, $C_{3-6}$ cycloalkyl and $C_{6-14}$ aryl group, each of which may be substituted by 1 to 5 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono- $C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-carbamoyl, di-$C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino,

(iv) a $C_{1-6}$ alkanoylamino group,

(v) a $C_{1-6}$ alkoxy group which may be substituted by 1 to 3 substituents selected from the group consisting of a halogen, nitro, cyano, hydroxy, an optionally halogenated $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, amino, mono-$C_{1-6}$ alkylamino, di-$C_{1-6}$ alkylamino, carboxyl, $C_{1-6}$ alkyl-carbonyl, $C_{1-6}$ alkoxy-carbonyl, carbamoyl, mono-$C_{1-6}$ alkyl-

carbamoyl, di-$C_{1-6}$ alkyl-carbamoyl, $C_{6-10}$ aryl-carbamoyl, $C_{6-10}$ aryl, $C_{6-10}$ aryloxy and an optionally halogenated $C_{1-6}$ alkyl-carbonylamino or

(vi) a $C_{1-3}$ alkylenedioxy group.

Claim 2 is dependent upon claim 1. The compound of claim 2 is ramelteon when:

$R^1$ is a $C_{1-6}$ alkyl group which is $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

$R^4$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

====== is a single bond;

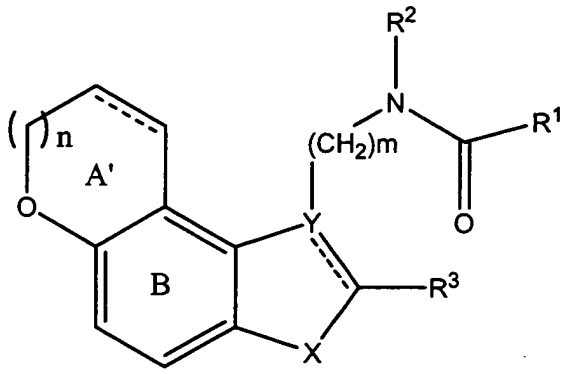
ring A is a 5 membered oxygen-containing heterocyclic group;

ring B is a benzene ring.

and m is the integer 2.

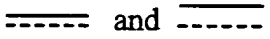
Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 2 covers the approved product.

Claim 4 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, which is a compound of the formula:




wherein ring A' is an optionally substituted, oxygen-containing heterocyclic ring;

n is an integer of 0 to 2;

 and  are independently a single bond or a double bond.

Claim 4 is dependent upon claim 1. The compound of the above formula is ramelteon when:

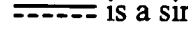
$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

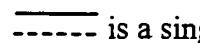
$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

 is a single bond;

 is a single bond;

ring A' is an oxygen-containing heterocyclic ring;

ring B is a benzene ring;

m is 2;

and n is the integer 0.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 4 covers the approved product.

CLAIM 5 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^1$ is

(i) an optionally substituted $C_{1-6}$ alkyl group,

(ii) an optionally substituted $C_{3-6}$ cycloalkyl group,

(iii) an optionally substituted $C_{2-6}$ alkenyl group,

(iv) an optionally substituted $C_{6-14}$ aryl group

(v) an optionally substituted mono- or di-$C_{1-6}$ alkylamino group;

(vi) an optionally substituted $C_{6-14}$ arylamino group or an optionally substituted 5- or 6-membered nitrogen-containing heterocyclic group.

Claim 5 is dependent upon claim 1. The compound of claim 5 is ramelteon when:

$R^1$ is a $C_{1-6}$ alkyl group which is $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

$R^4$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic group;

ring B is a benzene ring.

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 5 covers the approved product.

CLAIM 7 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^2$ is a hydrogen atom or an optionally substituted $C_{1-6}$ alkyl group.

Claim 7 is dependent upon claim 1. The compound of claim 7 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 7 covers the approved product.

CLAIM 8 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^2$ is a hydrogen atom.

Claim 8 is dependent upon claim 1. The compound of claim 8 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 8 covers the approved product.

CLAIM 9 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^3$ is a hydrogen atom or an optionally substituted hydrocarbon group.

Claim 9 is dependent upon claim 1. The compound of claim 9 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 9 covers the approved product.

CLAIM 10 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^3$ is a hydrogen atom.

Claim 10 is dependent upon claim 1. The compound of claim 10 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 10 covers the approved product.

CLAIM 11 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein $R^4$ is a hydrogen atom or an optionally substituted $C_{1-6}$ alkyl group.

Claim 11 is dependent upon claim 1. The compound of claim 11 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 11 covers the approved product.

CLAIM 12 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein X is $CHR^4$.

Claim 12 is dependent upon claim 1. The compound of claim 12 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 12 covers the approved product.

CLAIM 13 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein X is $CHR^4$ and ------ is a single bond.

Claim 13 is dependent upon claim 1. The compound of claim 13 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 13 covers the approved product.

CLAIM 14 of United States Patent No. 6,034,239 claims a compound as claimed in claim 13, wherein X is $CH_2$.

Claim 14 is dependent upon claim 13, which itself is dependent upon claim 1. The compound of claim 14 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CH_2$;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 14 covers the approved product.

CLAIM 16 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein Y is C or CH.

Claim 16 is dependent upon claim 1. The compound of claim 16 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

====== is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 16 covers the approved product.

CLAIM 17 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein Y is CH.

Claim 17 is dependent upon claim 1. The compound of claim 17 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 17 covers the approved product.

CLAIM 18 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein m is 2.

Claim 18 is dependent upon claim 1. The compound of claim 18 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 18 covers the approved product.

CLAIM 19 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein ring A is a tetrahydrofuran ring.

Claim 19 is dependent upon claim 1. The compound of claim 19 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a tetrahydrofuran ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 19 covers the approved product.

CLAIM 20 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein ring A is unsubstituted.

Claim 20 is dependent upon claim 1. The compound of claim 20 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is an unsubstituted 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 20 covers the approved product.

CLAIM 21 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, wherein ring B is unsubstituted.

Claim 21 is dependent upon claim 1. The compound of claim 21 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is an unsubstituted 5 membered oxygen-containing heterocyclic ring;

ring B is an unsubstituted benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 21 covers the approved product.

CLAIM 22 of United States Patent No. 6,034,239 claims a compound as claimed in claim 4, wherein n is 0.

Claim 22 is dependent upon claim 4, which is itself dependent upon claim 1. The compound of the above formula is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

 is a single bond;

 is a single bond;

ring A' is an oxygen-containing heterocyclic ring;

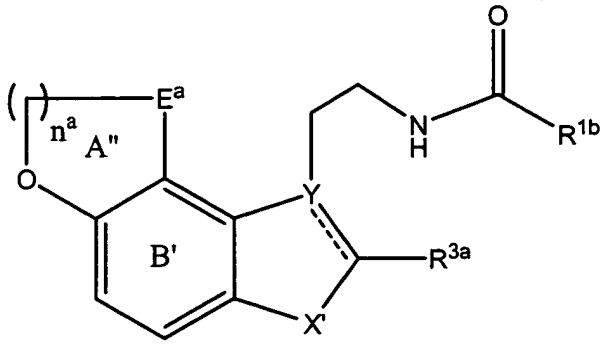
ring B is a benzene ring;

m is 2;

and n is the integer 0.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 22 covers the approved product.

Claim 23 of United States Patent No. 6,034,239 claims a compound as claimed in claim 1, which is a compound of the formula:




wherein $R^{1b}$ is $C_{1-6}$ alkyl,

X' is $CH_2$, NH or NCHO,

⚌ is a single bond or a double bond,

$R^{3a}$ is a hydrogen atom or phenyl,

$E^a$ is $CH_2CH_2$, CH=CH, $CH_2O$, CH=N, CONH or $CH_2HN$,

$n^a$ is 0 or 1,

ring A'' is a 5- or 6-membered oxygen-containing heterocyclic ring which may be substituted by 1 or 2 $C_{1-6}$ alkyl optionally substituted by a hydroxy, and

ring B' is a benzene ring which may be substituted by a halogen.

Claim 23 is dependent upon claim 1. The compound of the above formula is ramelteon when:

$R^{1b}$ is a $C_{1-6}$ alkyl group of the formula $C_2H_5$;

X' is $CH_2$;

⚌ is a single bond;

$R^{3a}$ is a hydrogen atom;

$E^a$ is $CH_2CH_2$;

$n^a$ is 0;

ring A'' is a 5-membered oxygen-containing heterocyclic ring; and

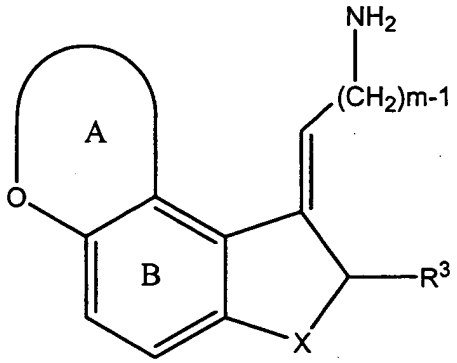
ring B' is a benzene ring.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 23 covers the approved product.

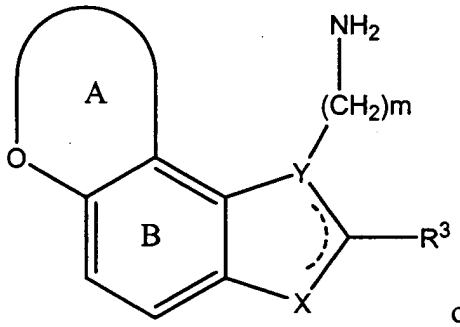
CLAIM 25 of United States Patent No. 6,034,239 claims a compound claimed in claim 1 which is (S)-N-[2-(1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl)ethyl]propionamide.

Claim 25 is dependent upon claim 1. This compound is ramelteon. The approved product ROZEREM™ contains ramelteon as the active ingredient. Please refer to the Chemical description of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. Thus claim 25 covers the approved product.

CLAIM 30 of United States Patent No. 6,034,239 claims a process for producing a compound as claimed in claim 1, which comprises reacting a compound of the formula (i):




or a salt thereof, or (ii) :




or a salt thereof, with a compound of the formula:

$R^1COOH$

or a salt or a reactive derivative thereof; and

if necessary, subjecting the resultant compound to reduction and/or alkylation.

Claim 30 is dependent upon claim 1. The method of claim 30 produces ramelteon when:

$R^1$ is a $C_{1-6}$ alkyl group which is $C_2H_5$;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

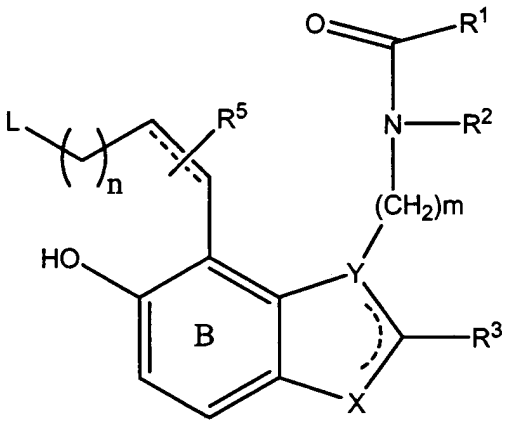
ring A is a 5 membered oxygen-containing heterocyclic group;

ring B is a benzene ring.

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 30 covers a method for producing the approved product.

CLAIM 31 of United States Patent No. 6,034,239 claims a process for producing a compound as claimed in claim 4, which comprises subjecting to cyclization a compound of the formula:




wherein $R^5$ represents a hydrogen atom, a halogen atom, an optionally substituted hydrocarbon group, an optionally substituted alkoxy group, a hydroxy group, a nitro group, a cyano group or an optionally substituted amino group; L represents a leaving group, or a salt thereof; and

if necessary subjecting the resultant compound to reduction.

Claim 31 is dependent upon claim 4, which itself is dependent upon claim 1. The method of claim 31 produces ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

$R^5$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

$\equiv\equiv\equiv$ is a single bond;

$\overline{\quad\quad}$ is a single bond;

ring B is a benzene ring;

m is 2;

n is the integer 0 and

L is a leaving group.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. Thus claim 31 covers a method for producing the approved product.

CLAIM 34 of United States Patent No. 6,034,239 claims a pharmaceutical composition which comprises a compound as claimed in claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

Claim 34 is dependent upon claim 1. The pharmaceutical composition of claim 34 comprises ramelteon when in the formula of claim 1:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ is a pharmaceutical composition which contains ramelteon as the active ingredient. Thus claim 34 covers the approved product.

CLAIM 35 of United States Patent No. 6,034,239 claims a composition as claimed in claim 34 wherein said compound or said pharmaceutically acceptable salt has a binding affinity for melatonin receptor.

Claim 35 is dependent upon claim 34, which itself is dependent upon claim 1. The pharmaceutical composition of claim 35 comprises ramelteon when in the formula of claim 1:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the CMC information on ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ is a pharmaceutical composition which contains ramelteon as the active ingredient. Thus claim 35 covers the approved product.

CLAIM 36 of United States Patent No. 6,034,239 claims a method for treating or preventing diseases related to the action of melatonin in mammals which comprises administrating to a subject in need thereof a therapeutically effective amount of a composition as claimed in claim 35.

Claim 36 is dependent upon claim 35, which itself is ultimately dependent upon claim 1. Claim 36 covers the administration of ramelteon for the treatment of insomnia characterized by delayed sleep onset. The mechanism of action for ramelteon for treating insomnia is described as being via the melatonin receptor.

Please refer to the CMC information on ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved

product ROZEREM™ is a pharmaceutical composition which contains ramelteon as the active ingredient and which acts on the melatonin receptor. Thus claim 35 covers a method of using the approved product.

CLAIM 40 of United States Patent No. 6,034,239 claims a method as claimed in claim 36 for treating or preventing sleep disorders.

Claim 40 is dependent upon claim 36, which itself is ultimately dependent upon claim 1. Claim 40 covers the administration of ramelteon for the treatment of insomnia characterized by delayed sleep onset. Insomnia is a sleep disorder.

Please refer to the CMC information on ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ is a pharmaceutical composition which contains ramelteon as the active ingredient and is used for treating the sleep disorder which is insomnia. Thus claim 40 covers a method of using the approved product.

CLAIM 41 of United States Patent No. 6,034,239 claims a process of manufacturing a pharmaceutical composition comprising the steps of selecting a compound or pharmaceutically acceptable salt of claim 1 and admixing said compound or salt with a pharmaceutically acceptable carrier.

A compound of claim 1 is ramelteon when:

$R^1$ is a hydrocarbon group of the formula $C_2H_5$;

$R^2$ is a hydrogen atom;

$R^3$ is a hydrogen atom;

X is $CHR^4$ where $R^4$ is a hydrogen atom;

Y is CH;

------ is a single bond;

ring A is a 5 membered oxygen-containing heterocyclic ring;

ring B is a benzene ring;

and m is the integer 2.

Please refer to the Chemical Structure of ramelteon shown in section 1.1 of EXHIBIT C and the label section of the approval letter EXHIBIT D. The approved product ROZEREM™ contains ramelteon as the active ingredient. The claimed process covers a method of making the approved product containing ramelteon. Thus claim 41 covers a method for making the approved product.

(10) The relevant dates and information pursuant to 35 U.S.C. §156(g) in order for the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows.

(a) The effective date of the investigational new drug ("IND") application for ROZEREM™ (ramelteon) Tablets, and the date of exemption under subsection 505(i) of the Federal Food, Drug and Cosmetic Act for ROZEREM™ (ramelteon) is May 5, 1999, i.e. 30 days after receipt of the IND application by the Secretary of Health and Human Services on April 5, 1999. The IND number assigned to the application is 58,136. See EXHIBIT G attached hereto. We note that the original sponsor of the IND was Takeda America Research & Development Center, Inc. a wholly owned subsidiary of TAKEDA, which was subsequently merged into another wholly owned subsidiary and the IND transferred to this entity, Takeda Pharmaceuticals America, Inc. The FDA was notified by letters dated August 11, 2000 and August 18, 2000. Please see EXHIBIT H1 and H2 attached hereto. Takeda Pharmaceuticals America, Inc. subsequently changed names to Takeda Pharmaceuticals North America, Inc. and the FDA was informed of the change of name by letter dated January 2, 2001. See Exhibit H3. The IND was subsequently transferred from Takeda Pharmaceuticals North America, Inc. to another wholly owned subsidiary, Takeda Global Research & Development, Inc. as the current IND sponsor on January 9, 2004. See EXHIBIT I.

(b) The date on which the new drug application ("NDA") on ROZEREM™ (ramelteon) was initially submitted under section 505 of the Federal Food, Drug and Cosmetic Act is September 22, 2004. The NDA number assigned to the application is NDA 21-782. See EXHIBIT J attached hereto. We note that the

original tradename submitted with respect to NDA 21-782 was LUNIVIA™. After submission, this name was subsequently changed to the currently approved ROZEREM™.

(c) The date on which the NDA application was approved is July 22, 2005. See EXHIBIT D attached hereto.

(11) A brief description of the significant activities undertaken by and or for the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities is attached hereto as EXHIBIT K.

(12) Applicant is of the opinion that United States Patent No. 6,034,239 is eligible for an extension under 35 U.S.C. §156, and the length of extension claimed is 808 days, based upon an expiration date of said patent of May 6, 2017 under 35 U.S.C. §154. The extension that is sought would extend the term of said patent to July 22, 2019, the maximum extended term allowed under 35 U.S.C. §156(c)(4).

The requirements of 35 U.S.C. §156(a) and 37 C.F.R. §1.720(c) have been satisfied as follows.

(a) U.S. Patent No. 6,034,239 claims a product as defined in 37 C.F.R. §1.710, ramelteon, which is the active ingredient in the approved product ROZEREM™.

(b) U.S. Patent No. 6,034,239 is not yet expired. As noted above, U.S. Patent No. 6,034,239 is not subject to any disclaimer.

(c) The term of U.S. Patent No. 6,034,239 has never been extended.

(d) This application for extension is being submitted by TAKEDA PHARMACUTICAL COMPANY LTD., the owner of record of U.S. Patent No. 6,034,239, through its attorneys and agents, in accordance with the requirements of 35 U.S.C. §156(d).

(e) The approved product ROZEREM™, has been subject to a regulatory review period under section 505 of the Federal Food, Drug and Cosmetic Act before its commercial marketing or use, and permission for said commercial marketing or use is the first permitted commercial marketing or use of the product and the active ingredient of the product, ramelteon, under the Federal Food, Drug and Cosmetic Act.

(f) No patent has to this date been extended, nor has any other extension been applied for, for the regulatory review period which forms the basis for this application for extension of the term of U.S. Patent No. 6,034,239

The length of extension of the term of U.S. Patent No. 6,034,239 of 808 days claimed by applicant, based upon the expiration date of said patent of March 6, 2017, and providing an extended patent term to expire July 22, 2019, is determined according to the provisions of 37 C.F.R. §1.775 as follows.

(a) According to 37 C.F.R. §1.775(b), the length of extension is equal to the regulatory review period for the approved product, reduced as appropriate according to paragraphs (d)(1) through (d)(6) of 37 C.F.R. §1.775.

(b) According to 37 C.F.R. §1.775(c), the regulatory review period is the sum of (1) the number of days in the period beginning on the date on which the exemption under section 505(i) of the Federal Food, Drug and Cosmetic Act became effective and ending on the date the NDA was initially submitted under section 505 and (2) the number of days in the period beginning on the date the NDA was initially submitted and ending on the date the NDA was approved.

The exemption under subsection 505(i) became effective on May 5, 1999, the NDA was initially submitted on September 21, 2004 and the NDA was approved July 22, 2005. Hence the regulatory review period is the sum of the periods from (1) May 5, 1999 to September 21, 2004 and (2) September 21, 2004 to July 22, 2005. This is the sum of (1) 1,967 days and (2) 305 days, which is 2272 days.

(c) According to 37 C.F.R. §1.775(d)(1)(i), the number of days in the review periods of paragraphs 37 C.F.R. §1.775(c)(1) and (c)(2) which were on or before the date on which the patent issued must be subtracted.

U.S. Patent No. 6,034,239 issued on March 7, 2000. The regulatory review period of 37 C.F.R. §1.775(c)(1) began on May 5, 1999, before the date of issue of the patent. Therefore 308 days must be subtracted from the previously determined 1,967 days of period (1), which yields an adjusted total of 1,659 days.

The submission of the application for approval under section 505 of the Federal Food, Drug and Cosmetic Act was made September 21, 2004, after the date on which the patent issued, and thus no reduction of the period determined under 37 C.F.R. §1.775(c)(2) is required.

(d) 37 C.F.R. §1.775(d)(1)(ii) does not apply.

(e) According to 37 C.F.R. §1.775(d)(1)(iii), the regulatory review period must then be reduced by one-half of the days remaining in the period defined in 37 C.F.R. §1.775(c)(1). This is one-half of the calculated 1,659 days of period (1), which is 829.5 days. Ignoring the half-day, this now leaves after subtraction a remaining period of 830 days. The resulting reduced regulatory review period is now the sum of (1) 830 days and (3) 305 days, which is 1,135 days. The reduced regulatory review period of 1,135 days is then added to the original expiration date of U.S. Patent No. 6,034,239 of March 6, 2017 to arrive at an extended patent term of April 15, 2020.

(f) As stated previously, no disclaimer applies to U.S. Patent No. 6,034,239, therefore, no reduction under 37 C.F.R. §1.775(d)(2) is required, keeping the calculated extended expiration date as April 15, 2020.

(g) According to 37 C.F.R. §1.775(d)(3), fourteen (14) years are added to the date of approval of the application to market ROZEREM™ (ramelteon) under section 505 of the Federal Food, Drug, and Cosmetic Act, July 22, 2005. This gives a date of July 22, 2019.

(h) The date determined under 37 C.F.R. §1.775(d)(2), April 15, 2020, is then compared to date determined under 37 C.F.R. §1.775(d)(3), July 22, 2019, and the earlier of the two selected. The selected extended expiration date is thus July 22, 2019.

(i) According to 37 C.F.R §1.775(d)(5), five (5) years are added to the original expiration date of United States Patent No. 6,034,239, March 6, 2017, giving the date of March 6, 2022. The date determined under 37 C.F.R. §1.775(d)(5), March 6, 2022, is then compared to date determined under 37 C.F.R. §1.775(d)(3), July 22, 2019, and the earlier of the two selected. The selected extended expiration date is thus July 22, 2019. Thus the reduced regulatory review period is the period between March 6, 2017 and July 22, 2019, which is 808 days.

(13) Applicant acknowledges a duty to disclose to the Director of the United States Patent and Trademark Office, the Secretary of Health and Human Services, or the Secretary of Agriculture, any information that is material to the determination of

entitlement to the extension being sought to the term of United States Patent No. 6,034,239.

(14) The Commissioner is authorized to charge the prescribed fee under 37 C.F.R. §1.20(j), for receiving and acting on this application for extension to USPTO Deposit Account No. 500,799, or any other required fees, and to credit any overpayment thereto.

(15) Please address all inquiries and correspondence relating to this application for patent term extension to:

Mark Chao, PhD, JD
Takeda Pharmaceuticals North America, Inc.
475 Half Day Road
Lincolnshire, Illinois 60069 USA
Tel: (847) 383-3372 Fax: (847) 383-3409

Two duplicate copies (2 copies) of these application papers, certified as such, are enclosed herewith.

Respectfully submitted,

Takeda Pharmaceutical Company Ltd.

Dated: September 6, 2005

By: _____

(847)383-3372
(847)383-3391

Mark Chao, Ph.D., Reg. No. 37,293
Elaine M. Ramesh, Ph.D., Reg. No. 43,032
Attorney Representatives for Applicant
Customer No. 23115

Takeda Pharmaceuticals North America, Inc.
Intellectual Property Department
475 Half Day Road
Lincolnshire, IL 60069 USA

**List of Exhibits**

A. A1) Copy of recorded assignment of the U.S. patent application which gave rise to United States Patent No. 6,034,239 from the inventors to Takeda Chemical Industries, Inc. and A2) A copy of the USPTO Notice of Recordation of Assignment.

B. Copy of USPTO Notice of Recordation of name change from Takeda Chemical Industries, Inc. to Takeda Pharmaceutical Company Ltd.

C. Chemical Characteristics and Identification of the Active Ingredient of ROZEREM™ (ramelteon).

D. Copy of FDA letter granting approval of NDA to market ROZEREM™ (ramelteon), letter dated July 22, 2005.

E. Complete copy of United States Patent No. 6,034,239.

F. Copy of the USPTO Maintenance Fee Statement for U.S. Patent 6,034,239.

G. Copy of letter acknowledging the receipt of the IND 58,136 for ramelteon by the FDA on April 5, 1999.

H. H1) Copy of letter from Takeda America Research & Development Company, Inc. to FDA informing the agency of pending transfer of IND to Takeda Pharmaceuticals America, Inc. dated August 11, 2000. H2) Copy of letter from Takeda Pharmaceuticals America, Inc. to FDA informing the agency of pending transfer of IND from Takeda America Research & Development Company, Inc. dated August 18, 2000. H3) Copy of letter from Takeda Pharmaceuticals North America, Inc. to the FDA informing the agency of the name change of the IND holder from Takeda Pharmaceuticals America, Inc. to Takeda Pharmaceuticals North America, Inc., dated January 2, 2001.

I. Copy of the letter from Takeda Pharmaceuticals North America, Inc. to the FDA informing the agency of the pending transfer of the IND to Takeda Global Research and Development, Inc. dated January 9, 2004.

J. Copy of letter acknowledging the receipt of NDA 21-782 for LUNIVIA™ (ramelteon), subsequently renamed as ROZEREM™ (ramelteon), by the FDA on September 22, 2004.

K. Brief Summary of the significant activities undertaken and the significant dates thereof, by and or for the marketing applicant during the applicable regulatory review period. K1) IND related activities. K2) NDA related activities.

# EXHIBIT A.

A1) A copy of recorded assignment of the U.S. patent application which gave rise to United States Patent No. 6,034,239 from the inventors to Takeda Chemical Industries, Inc.

# *ASSIGNMENT*

FOR VALUE RECEIVED, I/We, SHIGENORI OHKAWA, OSAMU UCHIKAWA, KOHJI FUKATSU and MASAOMI MIYAMOTO, (a) citizen(s) of JAPAN, residing (respectively) at: 45-20, Makamicho 6-chome, Takatsuki, Osaka 569, Japan; 15-16 Kozukayama 2-chome, Tarumi-ku, Kobe, Hyogo 655, Japan; 8-4, Tsukushigaoka 5-chome, Kita-ku, Kobe, Hyogo 651-12, Japan; and 12-11, Gotenyama 4-chome, Takarazuka, Hyogo 665, Japan, hereby sell, assign, transfer and convey unto

TAKEDA CHEMICAL INDUSTRIES, LTD.,

a corporation of Japan, having a place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 541, Japan, its successors, assigns and legal representatives (hereinafter called the "Assignee"), the entire right, title and interest, for the United States, in and to certain inventions relating to

TRICYCLIC COMPOUNDS, THEIR PRODUCTION AND USE

and described in an application for Letters Patent of the United States executed by me/us on even date herewith and in and to said application, and all divisions, renewals and continuations thereof, and all Letters Patent of the United States which may be granted, thereon, and all reissues and extensions thereof; and I/We hereby authorize and request the Commissioner of Patents and Trademarks of the United States to issue all Letters Patent upon said inventions to the Assignee or to such nominees as it may designate.

AND I/We authorize and empower the said Assignee or nominees to invoke and claim for any application for patent or other form of protection for said inventions filed by it or them, the benefit of the right of priority provided by the International Convention for the Protection of Industrial Property, as amended, or by any convention which may henceforth be substituted for it, and to invoke and claim such right of priority without further written or oral authorization from me/us.

AND I/We hereby consent that a copy of this assignment shall be deemed a full legal and formal equivalent of any assignment, consent to file or like document which may be required in the United States for any purpose and more particularly in proof of the right of said Assignee or nominees to claim the aforesaid benefit of the right of priority provided by the International Convention for the Protection of Industrial Property, as amended, or by any convention which may henceforth be substituted therefor.

AND I/We hereby covenant that I/We have the full right to convey the entire right, title and interest herein assigned and that we have not executed and will not execute any agreement in conflict herewith.

AND I/We hereby covenant and agree that I/We will communicate to said Assignee or nominees all facts known to me/us pertaining to said inventions, and testify in all legal proceedings, sign all lawful papers, execute all divisional, continuing and reissue applications, make all rightful oaths and declarations and in general perform all lawful acts necessary or proper to aid said Assignee or nominees in obtaining, maintaining and enforcing all lawful patent protection for said inventions in the United States.

IN TESTIMONY WHEREOF, I/We have hereunto set my/our hand(s) and seal(s) on the date(s) indicated below.

Assignor(s):

March 3, 1997 (Date)
Shigenori Ohkawa L.S.
SHIGENORI OHKAWA

March 3, 1997 (Date)
Osamu Uchikawa L.S.
OSAMU UCHIKAWA

March 3, 1997 (Date)
Kohji Fukatsu L.S.
KOHJI FUKATSU

March 3, 1997 (Date)
Masaomi Miyamoto L.S.
MASAOMI MIYAMOTO

Witness:

Kiyomi Nakano

A2) A copy of USPTO Notice of Recordation of Assignment.

UNITED STATES DEPARTMENT OF COMMERCE
**Patent and Trademark Office**
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

MAY 22, 1997

PTAS

FITZPATRICK, CELLA, HARPER & SCINTO
LAWRENCE S. PERRY
277 PARK AVENUE
NEW YORK, NEW YORK 10172-0194

*100390403A*

LSP
92.2379

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RECORDATION DATE: 03/06/1997

REEL/FRAME: 8433/0452
NUMBER OF PAGES: 2

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
OHKAWA, SHIGENORI

DOC DATE: 03/03/1997

ASSIGNOR:
UCHIKAWA, OSAMU

DOC DATE: 03/03/1997

ASSIGNOR:
FUKATSU, KOHJ

DOC DATE: 03/03/1997

ASSIGNOR:
MIYAMOTO, MASAOMI

DOC DATE: 03/03/1997

ASSIGNEE:
TAKEDA CHEMICAL INDUSTRIES, LTD.
1-1, DOSHOMACHI 4-CHOME, CHUO-KU
OSAKA 541, JAPAN

SERIAL NUMBER: 08812168
PATENT NUMBER:

FILING DATE:
ISSUE DATE:

JOANN STEWART, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

# EXHIBIT B.

A copy of USPTO Notice of Recordation of name change from Takeda Chemical Industries, Inc. to Takeda Pharmaceutical Company Ltd.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

JANUARY 27, 2005

PTAS *500018564A*

DAVID J. CUSHING
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

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RECORDATION DATE: 01/19/2005 REEL/FRAME: 015612/0101
NUMBER OF PAGES: 13

BRIEF: CHANGE OF NAME (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:
TAKEDA CHEMICAL INDUSTRIES, LTD. DOC DATE: 06/29/2004

ASSIGNEE:
TAKEDA PHARMACEUTICAL COMPANY,
LIMITED
1-1, DOSHOMACHI 4-CHOME
CHUO-KU, OSAKA, JAPAN

SERIAL NUMBER: 06779975 FILING DATE: 09/25/1985
PATENT NUMBER: 4612364 ✓ ISSUE DATE: 09/16/1986
TITLE: METHOD FOR PRODUCING FORMED PRODUCT OF HIGH MOLECULAR COMPOUNDS

SERIAL NUMBER: 06751672 FILING DATE: 07/03/1985
PATENT NUMBER: 4677191 ✓ ISSUE DATE: 06/30/1987
TITLE: COPOLYMER AND METHOD FOR PRODUCING THE SAME

015612/0101 PAGE 14

SERIAL NUMBER: 08762125 FILING DATE: 12/09/1996
PATENT NUMBER: 5977132 ✓ ISSUE DATE: 11/02/1999
TITLE: PROLACTIN PRODUCTION INHIBITORY AGENT

SERIAL NUMBER: 08813986 FILING DATE: 03/10/1997
PATENT NUMBER: 6004954 ✓ ISSUE DATE: 12/21/1999
TITLE: CONDENSED THIAZINE DERIVATIVES, THEIR PRODUCTION AND USE THEREOF

SERIAL NUMBER: 08902233 FILING DATE: 07/29/1997
PATENT NUMBER: 6013784 ✓ ISSUE DATE: 01/11/2000
TITLE: HST 2 MUTEINS, PHARMACEUTICAL COMPOSITIONS AND KITS COMPRISING SAME

SERIAL NUMBER: 08910691 FILING DATE: 08/13/1997
PATENT NUMBER: 6015552 ✓ ISSUE DATE: 01/18/2000
TITLE: USE OF NERVE GROWTH FACTOR-2 (NGF-2)/NEUROTROPHIN-3 TO PROMOTE LEUKOCYTE PROLIFERATION

SERIAL NUMBER: 08894317 FILING DATE: 08/14/1997
PATENT NUMBER: 6015789 ✓ ISSUE DATE: 01/18/2000
TITLE: COMBINED USE OF GNRH AGONIST AND ANTAGONIST

SERIAL NUMBER: 09063893 FILING DATE: 04/22/1998
PATENT NUMBER: 6020464 ✓ ISSUE DATE: 02/01/2000
TITLE: AN ISOLATED SMAD PROTEIN

SERIAL NUMBER: 09044536 FILING DATE: 03/19/1998
PATENT NUMBER: 6025467 ✓ ISSUE DATE: 02/15/2000
TITLE: PARATHYROID HORMONE DERIVATIVES AND THEIR USE

SERIAL NUMBER: 08812168 FILING DATE: 03/06/1997
PATENT NUMBER: 6034239 ✓ ISSUE DATE: 03/07/2000
TITLE: TRICYCLIC COMPOUNDS, THEIR PRODUCTION AND USE

SERIAL NUMBER: 09154164 FILING DATE: 09/16/1998
PATENT NUMBER: 6036976 ✓ ISSUE DATE: 03/14/2000
TITLE: SUSTAINED RELEASE MICROSPHERES AND PREPARATION THEREOF

SERIAL NUMBER: 09207043 FILING DATE: 12/08/1998
PATENT NUMBER: 6040324 ✓ ISSUE DATE: 03/21/2000
TITLE: PROPHYLACTIC OR THERAPEUTIC DRUG FOR RENAL DISEASES

SERIAL NUMBER: 08704991 FILING DATE: 08/29/1996
PATENT NUMBER: 6045830 ✓ ISSUE DATE: 04/04/2000
TITLE: METHOD OF PRODUCTION OF SUSTAINED-RELEASE PREPARATION

SERIAL NUMBER: 08682442 FILING DATE: 07/17/1996
PATENT NUMBER: 6048863 ✓ ISSUE DATE: 04/11/2000
TITLE: CONDENSED-RING THIOPHENE DERIVATIVES AND THIENOPYRIMIDINE DERIVATIVES, THEIR PRODUCTION AND USE

SERIAL NUMBER: 08530373 FILING DATE: 10/13/1995
PATENT NUMBER: 6051240 ✓ ISSUE DATE: 04/18/2000
TITLE: METHOD OF SEPARATING PROTECTIVE COMPONENTS OF BORDETELLA PERTUSSIS